RCE
1632

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Tomoki TODO et al.

Title: USE OF SOLUBLE COSTIMULATORY FACTOR FOR TUMOR IMMUNO-GENE THERAPY

Appl. No.: 09/679,147

Filing Date: 10/05/2000

Examiner: Anne Marie Sabrina Wehbe

Art Unit: 1632

PRELIMINARY REMARKS

Commissioner for Patents
Mail Stop RCE
Washington, D.C. 20231

Sir:

Applicants file this Preliminary Remarks for the Examiner's consideration to supplement the Preliminary Amendment submitted in our Request for Continued Examination under 37 C.F.R. §1.114 filed on June 16, 2003.

The Examiner has previously stated that the claims are only enabled for administering the vector into the tumor. Applicants urge reconsideration on the grounds that *in vivo* models have demonstrated that the herpes simplex virus can effectively target a tumor when the virus is not administered directly or locally to the tumor. The non-local targeting of tumors by herpes simplex virus has been well established. Moreover, the degree of experimentation, if any, that one of skill in the art would have needed to practice the present invention, would have simply involved injecting the HSV vector into various locations in a model to determine its efficacy. A claim is enabled even if routine experimentation is required to practice the invention. Lack of enablement is only found when the degree of experimentation is undue.

Applicants have attached hereto references evidencing the effectiveness of the HSV vector when it is not administered directly into a tumor but by systemic delivery. For example, Kooby describes effective delivery of G207, a type of HSV, by both direct tumor injection and regional vascular infusion. (Exhibit 1, abstract and p. 1327). Walker intravenously administered G207 by the tail vein and demonstrated "tumor growth inhibition, regression and eradication of distant prostrate cancers. (Exhibit 2, p. 2239 and 2241). Oyama demonstrated that intravenous injections into the tail of G207 inhibited tumor growth of bladder cancer. (Exhibit 3, abstract and p. 1685). Carew demonstrated the effectiveness of G207 via regional perfusion. (Exhibit 4, p. 1599). For mice that had pre-existing immunity to HSV, while Delman did find that route of viral administration did influence therapy, intravenous delivery did produce some detectable attenuation. (Exhibit, 5, abstract).

Moreover, one of skill in the art could have practiced intraperitoneal, intravesical or intrapleural administration of present invention. Bennett states that peritoneal delivery of G207 effectively kills tumor cells. (Exhibit 6, abstract). Cozzi effectively intravesically treated bladder cancer with both G207 and NV1020. (Exhibit 7, abstract). And, finally, Ebright demonstrated successful intrapleural administration of NV1020. (Exhibit 8, abstract.)

These references effectively demonstrated that the present invention was enabled from more than direct injection to the tumor. Therefore, withdrawal of the present rejection for lack of enablement is respectfully requested.

In view of the above remarks and amendments previously submitted, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. If the Examiner believes that an interview would advance prosecution of the application, he is invited to contact the undersigned by telephone.

If there are any unaccounted fees due in connection with the filing of this Amendment, please charge the fees to our Deposit Account No. 19-0741.

Respectfully submitted,

Date: June 19, 2003

By _____

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